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DATE: Friday, January 28, 2005

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		<i>DB=USPT; THES=ASSIGNEE; PLUR=YES; OP=ADJ</i>	
<input type="checkbox"/>	L8	L5 and CCR5	26
<input type="checkbox"/>	L7	L6 and (CC-CKR5)	3
<input type="checkbox"/>	L6	L5 and HIV	235
<input type="checkbox"/>	L5	L4	722
		<i>DB=PGPB,USPT,EPAB,JPAB,DWPI; THES=ASSIGNEE; PLUR=YES; OP=ADJ</i>	
<input type="checkbox"/>	L4	L3 and R5	2234
<input type="checkbox"/>	L3	antibody	204532
<input type="checkbox"/>	L2	L1 and CCR5	3
<input type="checkbox"/>	L1	Wu L.in.	789

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=> file caplus biosis

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FILE 'CAPLUS' ENTERED AT 06:43:09 ON 28 JAN 2005
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=> antibody

L1 989892 ANTIBODY

=> CCR5

L2 6393 CCR5

=> "CC CKR5"

L3 35 "CC CKR5"

=> L1 and L2

L4 1147 L1 AND L2

=> L1 (s) L2

L5 536 L1 (S) L2

=> L1 and L3

L6 7 L1 AND L3

=> D L6 IBIB ABS 1-6

=> L5 and 2D7

L7 33 L5 AND 2D7

=> L5 and inhibition

L8 73 L5 AND INHIBITION

=> L8 and HIV

L9 58 L8 AND HIV

L6 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:772659 CAPLUS
DOCUMENT NUMBER: 128:33766
TITLE: Methods of identifying G-coupled receptors associated
with macrophage-trophic HIV, and diagnostic and
therapeutic uses thereof
INVENTOR(S): Littman, Dan R.; Deng, Hongkui; Ellmeier, Wilfried;
Landau, Nathaniel R.; Liu, Rong
PATENT ASSIGNEE(S): New York University, USA
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9744055	A1	19971127	WO 1997-US8926	19970520
W:	AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, GH, HU, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
US 5939320	A	19990817	US 1996-666020	19960619
AU 9731434	A1	19971209	AU 1997-31434	19970520
PRIORITY APPLN. INFO.:			US 1996-17157P	P 19960520
			US 1996-650412	A 19960520
			US 1996-666020	A 19960619
			WO 1997-US8926	W 19970520

AB Entry of HIV-1 into target cells requires cell surface CD4 as well as addnl. host cell cofactors. A cofactor required for infection with virus adapted for growth in transformed T cell lines was recently identified and named fusin. Fusin, however, does not promote entry of macrophage-tropic viruses that are believed to be the key pathogenic strains in vivo. It has now been determined that the principal cofactor for entry mediated by the envelope glycoproteins of primary macrophage-tropic strains of HIV-1 is CC-CKR5, a receptor for the β -chemokines RANTES, MIP-1 α , and MIP-1 β . The cofactor is useful for screening of drugs capable of modulating the production of a translocation promoting agent and capable of treating AIDS.

L6 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:229024 CAPLUS

DOCUMENT NUMBER: 128:279581

TITLE: Cloning, sequence, and expression of a mouse genomic clone for the **CC-CKR5** receptor and construction of knockout mutations

INVENTOR(S): Bergsma, Derk J.; Brawner, Mary E.; Shabon, Usman

PATENT ASSIGNEE(S): Smithkline Beecham Corp., USA

SOURCE: Eur. Pat. Appl., 27 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 834564	A2	19980408	EP 1997-307823	19971003
EP 834564	A3	19980513		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6388055	B1	20020514	US 1996-724984	19961003
JP 10179180	A2	19980707	JP 1997-307784	19971003
PRIORITY APPLN. INFO.:			US 1996-724984	A 19961003

AB Mouse chemokine receptor **CC-CKR5** polypeptides and DNA (RNA) encoding such mouse **CC-CKR5** and a procedure for producing such polypeptides by recombinant techniques is disclosed. Also disclosed are methods for utilizing such mouse **CC-CKR5** in the development of gene knockout mice for use as a model for human immunodeficiency virus.. Expression vectors carrying the **CC-CKR5** gene are constructed and expressed in human embryonic kidney 293 cells. **Antibodies** to **CC-CKR5** are also claimed.

L6 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:499783 CAPLUS

DOCUMENT NUMBER: 135:103329

TITLE: Methods of identifying G protein-coupled receptors associated with the uptake of macrophage-trophic HIV, and their use in diagnosis and treatment of AIDS

INVENTOR(S): Littman, Dan R.; Deng, Hongkui; Ellmeier, Wilfried; Landau, Nathaniel R.; Liu, Rong

PATENT ASSIGNEE(S): The Aaron Diamond Aids Research Center, USA; New York University

SOURCE: U.S., 37 pp., Cont.-in-part of U.S. Ser. No. 858,660, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 6258527	B1	20010710	US 1997-861105	19970521
US 2003096221	A1	20030522	US 2000-734221	20001211
PRIORITY APPLN. INFO.:			US 1996-17157P	P 19960520
			US 1996-20043P	P 19960619
			US 1997-858660	B2 19970519
			US 1997-861105	A1 19970521

AB Entry of HIV-1 into target cells requires cell surface CD4 as well as addnl. host cell cofactors. A cofactor required for infection with virus adapted for growth in transformed T cell lines was recently identified and named fusin. Fusin, however, does not promote entry of macrophage-tropic viruses that are believed to be the key pathogenic strains in vivo. It has now been determined that the principal cofactor for entry mediated by the envelope glycoproteins of primary macrophage-tropic strains of HIV-1 is CC-CKR5, a receptor for the β -chemokines RANTES, MIP-1 α , and MIP-1 β . The uptake of the virus may be blocked by ligands for the receptor or by preventing the receptor gene expression and in control of the synergism between infection by other viruses and the spread of HIV into other cell types. Expts. with viruses pseudotyped with different env glycoproteins showed that uptake was dependent upon the presence of chemokine receptors with different serotypes of the virus showing different receptor requirements. Methods of using chemokine receptor-deficient host cells as expression hosts to identify receptor requirements of clin. isolates of HIV-1 are described.

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:185460 CAPLUS

DOCUMENT NUMBER: 132:333214

TITLE: **Inhibition of M-tropic HIV-1**
infection by the fd phage-gene 3 protein with
MIP-1 α -binding activity

AUTHOR(S): Meta, Akihiro; Torigoe, Naohiko; Ito, Yuji; Arakaki,
Rieko; Nakashima, Hideki; Sugimura, Kazuhisa

CORPORATE SOURCE: Department of Bioengineering, Faculty of Engineering,
Kagoshima University, Kagoshima, 890-0063, Japan

SOURCE: Molecular Immunology (2000), Volume Date 1999, 36(18),
1249-1254

CODEN: MOIMD5; ISSN: 0161-5890

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB CCR5 is a chemokine receptor with seven transmembrane-domains. It is expressed on T cells and macrophages and functions as the principal co-receptor for macrophage (M)-tropic strains of HIV-1. The anti-CCR5 monoclonal **antibody** (mAb) 2D7 inhibits the binding and chemotaxis of the three natural β -chemokine ligands of CCR5, macrophage inflammatory protein (MIP)-1 α , MIP-1 β , and RANTES, to CCR5+ cells. The mAb also efficiently blocks the infectivity of several M-tropic and dual-tropic HIV-1 strains in vitro. In this study, the authors attempted to determine the peptide motif recognized with the 2D7 mAb. The authors isolated phage clones by panning a phage display library using 2D7 and identified three peptide motifs. One of these phage clones (M23) showed a marked inhibitory activity on HIV-1 infection. The unique sequence of 15 amino acids with an internal disulfide bond was inserted in the g3p of the M23 phage clone (M23-g3p). The M23-g3p was purified by fast-performance liquid chromatog. (FPLC). The authors show here that (1) M23-g3p was specifically recognized with anti-CCR5 mAb; (2) M23-g3p showed inhibitory activity on the infectivity of M-tropic but not T-tropic HIV-1 strains; (3) M23-g3p bound to MIP-1 α , MIP-1 β , and RANTES but not MCP-1. These results suggested that the M23-g3p might mimic the CCR5-binding domain shared by β -chemokines, MIP-1 α , MIP-1 β , and RANTES as well as the HIV-1 infection.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:263464 CAPLUS

DOCUMENT NUMBER: 131:57557

TITLE: **Differential inhibition of human**
immunodeficiency virus type 1 fusion, gp120 binding,
and CC-chemokine activity by monoclonal
antibodies to CCR5

AUTHOR(S): ~~Olson~~, William C.; Rabut, Gwenael E. E.; Nagashima,
Kirsten A.; Tran, Diep N. H.; Anselma, Deborah J.;
Monard, Simon P.; Segal, Jeremy P.; Thompson, Daniah
A. D.; Kajumo, Francis; Guo, Yong; Moore, John P.;
Maddon, Paul J.; Dragic, Tatjana

CORPORATE SOURCE: Aaron Diamond AIDS Research Center, The Rockefeller
University, New York, NY, 10016, USA

SOURCE: Journal of Virology (1999), 73(5), 4145-4155

CODEN: JOVIAM; ISSN: 0022-538X

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The CC-chemokine receptor CCR5 mediates fusion and entry of the most commonly transmitted human immunodeficiency virus type 1 (HIV-1) strains. The authors have isolated 6 new anti-CCR5 murine

monoclonal **antibodies** (MAbs), designated PA8, PA9, PA10, PA11, PA12, and PA14. A panel of CCR5 alanine point mutants was used to map the epitopes of these MAbs and the previously described MAb 2D7 to specific amino acid residues in the N terminus and/or second extracellular loop regions of CCR5. This structural information was correlated with the MAbs' abilities to inhibit (1) **HIV-1** entry, (2) **HIV-1** envelope glycoprotein-mediated membrane fusion, (3) gp120 binding to CCR5, and (4) CC-chemokine activity. Surprisingly, there was no correlation between the ability of a MAb to inhibit **HIV-1** fusion-entry and its ability to inhibit either the binding of a gp120-soluble CD4 complex to CCR5 or CC-chemokine activity. MAbs PA9-PA12, whose epitopes include residues in the CCR5 N terminus, strongly inhibited gp120 binding but only moderately inhibited **HIV-1** fusion and entry and had no effect on RANTES-induced calcium mobilization. MAbs PA14 and 2D7, the most potent inhibitors of **HIV-1** entry and fusion, were less effective at inhibiting gp120 binding and were variably potent at inhibiting RANTES-induced signaling. With respect to inhibiting **HIV-1** entry and fusion, PA12 but not PA14 was potentially synergistic when used in combination with 2D7, RANTES, and CD4-IgG2, which inhibits **HIV-1** attachment. The data support a model wherein **HIV-1** entry occurs in 3 stages: receptor (CD4) binding, coreceptor (CCR5) binding, and coreceptor-mediated membrane fusion. These antibodies will be useful for further dissecting these events.

REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:683672 CAPLUS

DOCUMENT NUMBER: 127:357954

TITLE: Interaction of chemokine receptor CCR5 with its ligands: multiple domains for **HIV-1** gp120 binding and a single domain for chemokine binding

AUTHOR(S): Wu, Lijun; LaRosa, Greg; Kassam, Nasim; Gordon, Cynthia J.; Heath, Heidi; Ruffin, Nancy; Chen, Howard; Humblías, Jason; Samson, Michel; Parmentier, Marc; Moore, John P.; Mackay, Charles R.

CORPORATE SOURCE: LeukoSite, Inc., Cambridge, MA, 02142, USA

SOURCE: Journal of Experimental Medicine (1997), 186(8), 1373-1381

CODEN: JEMEAV; ISSN: 0022-1007

PUBLISHER: Rockefeller University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB CCR5 is a chemokine receptor expressed by T cells and macrophages, which also functions as the principal coreceptor for macrophage (M)-tropic strains of **HIV-1**. To understand the mol. basis of the binding of chemokines and **HIV-1** to CCR5, we developed a number of mAbs that inhibit the various interactions of CCR5, and mapped the binding sites of these mAbs using a panel of CCR5/CCR2b chimeras. One mAb termed 2D7 completely blocked the binding and chemotaxis of the three natural chemokine ligands of CCR5, RANTES (regulated on activation normal T cell expressed and secreted), macrophage inflammatory protein (MIP)-1 α , and MIP-1 β , to CCR5 transfectants. This mAb was a genuine antagonist of CCR5, since it failed to stimulate an increase in intracellular calcium concentration in the CCR5 transfectants, but blocked calcium responses elicited by RANTES, MIP-1 α , or MIP-1 β . This mAb inhibited most of the RANTES and MIP-1 α chemotactic responses of activated T cells, but not of monocytes, suggesting differential usage of chemokine receptors by these two cell types. The 2D7 binding site mapped to the second extracellular loop of CCR5, whereas a group of mAbs that failed to block chemokine binding all mapped to the NH2-terminal region of CCR5. Efficient inhibition of an M-tropic **HIV-1**-derived envelope glycoprotein gp120 binding to CCR5 could be achieved with mAbs recognizing either the second extracellular loop or the

NH2-terminal region, although the former showed superior **inhibition**. Addnl., **2D7** efficiently blocked the infectivity of several M-tropic and dual-tropic **HIV-1** strains in vitro. These results suggest a complicated pattern of **HIV-1** gp120 binding to different regions of CCR5, but a relatively simple pattern for chemokine binding. We conclude that the second extracellular loop of CCR5 is an ideal target site for the development of inhibitors of either chemokine or **HIV-1** binding to CCR5.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 5 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 2000:177648 BIOSIS
DOCUMENT NUMBER: PREV200000177648
TITLE: **Inhibition** of M-tropic **HIV-1** infection

by the fd phage-gene 3 protein with MIP-1alpha-binding activity.

AUTHOR(S): Meta, Akihiro; Torigoe, Naohiko; Ito, Yuji; Arakaki, Rieko; Nakashima, Hideki; Sugimura, Kazuhisa [Reprint author]

CORPORATE SOURCE: Department of Bioengineering, Faculty of Engineering, Kagoshima University, 1-21-40 Korimoto, Kagoshima, 890-0063, Japan

SOURCE: Molecular Immunology, (Dec., 1999) Vol. 36, No. 18, pp. 1249-1254. print.

CODEN: MOIMD5. ISSN: 0161-5890.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 11 May 2000

Last Updated on STN: 4 Jan 2002

AB CCR5 is a chemokine receptor with seven transmembrane-domains. It is expressed on T cells and macrophages and functions as the principal co-receptor for macrophage (M)-tropic strains of **HIV-1**. The anti-CCR5 monoclonal **antibody** (mAb) **2D7** inhibits the binding and chemotaxis of the three natural beta-chemokine ligands of CCR5, macrophage inflammatory protein (MIP)-1alpha, MIP-1beta, and RANTES, to CCR5+ cells. The mAb also efficiently blocks the infectivity of several M-tropic and dual-tropic **HIV-1** strains in vitro. In this study, we attempted to determine the peptide motif recognized with the **2D7** mAb. We isolated phage clones by panning a phage display library using **2D7** and identified three peptide motifs. One of these phage clones (M23) showed a marked inhibitory activity on **HIV-1** infection. The unique sequence of 15 amino acids with an internal disulfide bond was inserted in the g3p of the M23 phage clone (M23-g3p). The M23-g3p was purified by fast-performance liquid chromatography (FPLC). We show here that (1) M23-g3p was specifically recognized with anti-CCR5 mAb; (2) M23-g3p showed inhibitory activity on the infectivity of M-tropic but not T-tropic **HIV-1** strains; (3) M23-g3p bound to MIP-1alpha, MIP-1beta, and RANTES but not MCP-1. These results suggested that the M23-g3p might mimic the CCR5-binding domain shared by beta-chemokines, MIP-1alpha, MIP-1beta, and RANTES as well as the **HIV-1** infection.

L12 ANSWER 5 OF 5 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 1999:238925 BIOSIS
DOCUMENT NUMBER: PREV199900238925
TITLE: Differential **inhibition** of human immunodeficiency virus type 1 fusion, gp120 binding, and CC-chemokine activity by monoclonal **antibodies** to CCR5

AUTHOR(S): Olson, William C.; Rabut, Gwenael E. E.; Nagashima, Kirsten A.; Tran, Diep N. H.; Anselma, Deborah J.; Monard, Simon P.; Segal, Jeremy P.; Thompson, Daniah A. D.; Kajumo, Francis; Guo, Yong; Moore, John P.; Maddon, Paul J.; Dragic, Tatjana [Reprint author]

CORPORATE SOURCE: ✓ Aaron Diamond AIDS Research Center, 455 1st Ave., 7th
Floor, New York, NY, 10016, USA
SOURCE: Journal of Virology, (May, 1999) Vol. 73, No. 5, pp.
4145-4155. print.
CODEN: JOVIAM. ISSN: 0022-538X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Jun 1999
Last Updated on STN: 17 Jun 1999

AB The CC-chemokine receptor CCR5 mediates fusion and entry of the most commonly transmitted human immunodeficiency virus type 1 (**HIV-1**) strains. We have isolated six new anti-CCR5 murine monoclonal **antibodies** (MABs), designated PA8, PA9, PA10, PA11, PA12, and PA14. A panel of CCR5 alanine point mutants was used to map the epitopes of these MABs and the previously described MAB **2D7** to specific amino acid residues in the N terminus and/or second extracellular loop regions of CCR5. This structural information was correlated with the MABs' abilities to inhibit (i) **HIV-1** entry, (ii) **HIV-1** envelope glycoprotein-mediated membrane fusion, (iii) gp120 binding to CCR5, and (iv) CC-chemokine activity. Surprisingly, there was no correlation between the ability of a MAB to inhibit **HIV-1** fusion-entry and its ability to inhibit either the binding of a gp120-soluble CD4 complex to CCR5 or CC-chemokine activity. MABs PA9 to PA12, whose epitopes include residues in the CCR5 N terminus, strongly inhibited gp120 binding but only moderately inhibited **HIV-1** fusion and entry and had no effect on RANTES-induced calcium mobilization. MABs PA14 and **2D7**, the most potent inhibitors of **HIV-1** entry and fusion, were less effective at inhibiting gp120 binding and were variably potent at inhibiting RANTES-induced signaling. With respect to inhibiting **HIV-1** entry and fusion, PA12 but not PA14 was potently synergistic when used in combination with **2D7**, RANTES, and CD4-immunoglobulin G2, which inhibits **HIV-1** attachment. The data support a model wherein **HIV-1** entry occurs in three stages: receptor (CD4) binding, coreceptor (CCR5) binding, and coreceptor-mediated membrane fusion. The antibodies described will be useful for further dissecting these events.

L11 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:683672 CAPLUS

DOCUMENT NUMBER: 127:357954

TITLE: Interaction of chemokine receptor CCR5 with its
ligands: multiple domains for HIV-1 gp120 binding and
a single domain for chemokine binding

AUTHOR(S): Wu, Lijun; LaRosa, Greg; Kassam, Nasim; Gordon,
Cynthia J.; Heath, Heidi; Ruffin, Nancy; Chen, Howard;
Humblias, Jason; Samson, Michel; Parmentier, Marc;
Moore, John P.; Mackay, Charles R.

CORPORATE SOURCE: LeukoSite, Inc., Cambridge, MA, 02142, USA

SOURCE: Journal of Experimental Medicine (1997), 186(8),
1373-1381

CODEN: JEMEAV; ISSN: 0022-1007

PUBLISHER: Rockefeller University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

TI Interaction of chemokine receptor CCR5 with its ligands: multiple domains
for HIV-1 gp120 binding and a single domain for chemokine binding

AU Wu, Lijun; LaRosa, Greg; Kassam, Nasim; Gordon, Cynthia J.; Heath, Heidi;
Ruffin, Nancy; Chen, Howard; Humblias, Jason; Samson, Michel; Parmentier,
Marc; Moore, John P.; Mackay, Charles R.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:353334 CAPLUS
DOCUMENT NUMBER: 131:169077
TITLE: Peptide-motif analysis of phage clones selected by
anti-CCR5 monoclonal **antibody** (
2D7)
AUTHOR(S): Meta, Akihiro; Torigoe, Naohiko; Ito, Yuji; Arakaki,
Rieko; Nakashima, Hideki; Sugimura, Kazuhisa
CORPORATE SOURCE: Department of Bioengineering, Faculty of Engineering,
Kagoshima University, Kagoshima, 890-0065, Japan
SOURCE: Peptide Science (1999), Volume Date 1998, 35th,
489-492
CODEN: PSCIFQ; ISSN: 1344-7661
PUBLISHER: Protein Research Foundation
DOCUMENT TYPE: Journal
LANGUAGE: English
TI Peptide-motif analysis of phage clones selected by anti-CCR5
monoclonal **antibody** (2D7)
AU Meta, Akihiro; Torigoe, Naohiko; Ito, Yuji; Arakaki, Rieko; Nakashima,
Hideki; Sugimura, Kazuhisa
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

DOCUMENT NUMBER: 127:357954
TITLE: Interaction of chemokine receptor CCR5 with its
ligands: multiple domains for **HIV-1** gp120
binding and a single domain for chemokine binding
AUTHOR(S): Wu, Lijun; LaRosa, Greg; Kassam, Nasim; Gordon,
Cynthia J.; Heath, Heidi; Ruffin, Nancy; Chen, Howard;
Humblias, Jason; Samson, Michel; Parmentier, Marc;
Moore, John P.; Mackay, Charles R.
CORPORATE SOURCE: LeukoSite, Inc., Cambridge, MA, 02142, USA
SOURCE: Journal of Experimental Medicine (1997), 186(8),
1373-1381
CODEN: JEMEAV; ISSN: 0022-1007
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB CCR5 is a chemokine receptor expressed by T cells and macrophages, which also functions as the principal coreceptor for macrophage (M)-tropic strains of **HIV-1**. To understand the mol. basis of the binding of chemokines and **HIV-1** to CCR5, we developed a number of mAbs that inhibit the various interactions of CCR5, and mapped the binding sites of these mAbs using a panel of CCR5/CCR2b chimeras. One mAb termed **2D7** completely blocked the binding and chemotaxis of the three natural chemokine ligands of CCR5, RANTES (regulated on activation normal T cell expressed and secreted), macrophage inflammatory protein (MIP)-1 α , and MIP-1 β , to CCR5 transfectants. This mAb was a genuine antagonist of CCR5, since it failed to stimulate an increase in intracellular calcium concentration in the CCR5 transfectants, but blocked calcium responses elicited by RANTES, MIP-1 α , or MIP-1 β . This mAb inhibited most of the RANTES and MIP-1 α chemotactic responses of activated T cells, but not of monocytes, suggesting differential usage of chemokine receptors by these two cell types. The **2D7** binding site mapped to the second extracellular loop of CCR5, whereas a group of mAbs that failed to block chemokine binding all mapped to the NH2-terminal region of CCR5. Efficient **inhibition** of an M-tropic **HIV-1**-derived envelope glycoprotein gp120 binding to CCR5 could be achieved with mAbs recognizing either the second extracellular loop or the NH2-terminal region, although the former showed superior **inhibition**. Addnl., **2D7** efficiently blocked the infectivity of several M-tropic and dual-tropic **HIV-1** strains in vitro. These results suggest a complicated pattern of **HIV-1** gp120 binding to different regions of CCR5, but a relatively simple pattern for chemokine binding. We conclude that the second extracellular loop of CCR5 is an ideal target site for the development of inhibitors of either chemokine or **HIV-1** binding to CCR5.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ACCESSION NUMBER: 1999:263464 CAPLUS
DOCUMENT NUMBER: 131:57557
TITLE: Differential **inhibition** of human
immunodeficiency virus type 1 fusion, gp120 binding,
and CC-chemokine activity by monoclonal
antibodies to CCR5
AUTHOR(S): Olson, William C.; Rabut, Gwenael E. E.; Nagashima,
Kirsten A.; Tran, Diep N. H.; Anselma, Deborah J.;
Monard, Simon P.; Segal, Jeremy P.; Thompson, Daniah
A. D.; Kajumo, Francis; Guo, Yong; Moore, John P.;
Maddon, Paul J.; Dragic, Tatjana
CORPORATE SOURCE: Aaron Diamond AIDS Research Center, The Rockefeller
University, New York, NY, 10016, USA
SOURCE: Journal of Virology (1999), 73(5), 4145-4155
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The CC-chemokine receptor CCR5 mediates fusion and entry of the most commonly transmitted human immunodeficiency virus type 1 (**HIV-1**) strains. The authors have isolated 6 new anti-**CCR5** murine monoclonal **antibodies** (MABs), designated PA8, PA9, PA10, PA11, PA12, and PA14. A panel of CCR5 alanine point mutants was used to map the epitopes of these MABs and the previously described MAB **2D7** to specific amino acid residues in the N terminus and/or second extracellular loop regions of CCR5. This structural information was correlated with the MABs' abilities to inhibit (1) **HIV-1** entry, (2) **HIV-1** envelope glycoprotein-mediated membrane fusion, (3) gp120 binding to CCR5, and (4) CC-chemokine activity. Surprisingly, there was no correlation between the ability of a MAB to inhibit **HIV-1** fusion-entry and its ability to inhibit either the binding of a gp120-soluble CD4 complex to CCR5 or CC-chemokine activity. MABs PA9-PA12, whose epitopes include residues in the CCR5 N terminus, strongly inhibited gp120 binding but only moderately inhibited **HIV-1** fusion and entry and had no effect on RANTES-induced calcium mobilization. MABs PA14 and **2D7**, the most potent inhibitors of **HIV-1** entry and fusion, were less effective at inhibiting gp120 binding and were variably potent at inhibiting RANTES-induced signaling. With respect to inhibiting **HIV-1** entry and fusion, PA12 but not PA14 was potently synergistic when used in combination with **2D7**, RANTES, and CD4-IgG2, which inhibits **HIV-1** attachment. The data support a model wherein **HIV-1** entry occurs in 3 stages: receptor (CD4) binding, coreceptor (CCR5) binding, and coreceptor-mediated membrane fusion. These antibodies will be useful for further dissecting these events.

L6 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:459509 CAPLUS
DOCUMENT NUMBER: 127:173725
TITLE: Development of resistance of human immunodeficiency virus type 1 to dextran sulfate associated with the emergence of specific mutations in the envelope gp 120 glycoprotein
AUTHOR(S): Este, Jose A.; Schols, Dominique; De Vreese, Karen; Van Laethem, Kristel; Vandamme, Anne-Mieke; Desmyter, Jan; De Clercq, Erik
CORPORATE SOURCE: Rega Institute for Medical Research, Katholieke Universiteit Leuven, Louvain, B-3000, Belg.
SOURCE: Molecular Pharmacology (1997), 52(1), 98-104
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

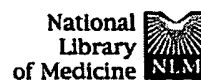
AB Polyanionic compds. are known to inhibit the binding of human immunodeficiency virus (HIV) to CD4+ cells and the subsequent fusion step between the virus and cells. An HIV-1 strain resistant to dextran sulfate (DS) was selected by cultivation of HIV-1 (NL4-3)-infected MT-4 cells in the presence of DS Mr 5000. DS did not inhibit the binding of DS-resistant virus to MT-4 cells or syncytium formation between MOLT cells and HUT-78 cells persistently infected with the DS-resistant virus. In addition, a monoclonal **antibody** with specificity for the V3 loop of envelope gp120 glycoprotein did not recognize the DS-resistant HIV-1 gp120 V3 loop. The following mutations were found in the gp120 mol. of the DS-resistant HIV-1 strain but not in the wild-type strain: S114N in the V1 loop region; S134N in the V2 loop region; K269E, Q278H, and N293D in the V3 loop region; N323S in the C3 region; a deletion of 5 amino acids (Phe-Asn-Ser-Thr-Trp) at positions 364-368 in the V4 loop; and R387I in the CD4 binding domain. These results suggest that (i) DS interacts with specific amino acid residues in the gp 120 mol., (ii) the virus is able to overcome the inhibitory effect of DS on viral infectivity, (iii) cross-resistance developed against those polyanionic compds. that are structurally related to DS, and (iv) the mol. determinants of HIV cell tropism, syncytium-inducing ability, coreceptor (fusin/CC-CKR5) utilization, and polyanion resistance seem to be located in the env genome of HIV and specifically in the V3 loop domain.

L6 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:433148 CAPLUS
DOCUMENT NUMBER: 125:112550
TITLE: Cell type-specific fusion cofactors determine human immunodeficiency virus type 1 tropism for T-cell lines versus primary macrophages
AUTHOR(S): Alkhatib, Ghalib; Broder, Christopher C.; Berger, Edward A.
CORPORATE SOURCE: Lab. Viral Dis., Natl. Inst. Allergy and Infectious Dis., Bethesda, MD, 20892, USA
SOURCE: Journal of Virology (1996), 70(8), 5487-5494
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Work in this laboratory previously demonstrated that the tropism of different human immunodeficiency type 1 isolates for infection of human CD4+ continuous cell lines (e.g., T-cell lines and HeLa-CD4 transformants) vs. primary macrophages is associated with parallel intrinsic fusogenic specificities of the corresponding envelope glycoproteins (Envs). For T-cell line-tropic isolates, it is well established that the target cell must also contain a human-specific fusion cofactor(s) whose identity is unknown. In this study, we tested the hypothesis that the Env fusion specificities underlying T-cell line vs. macrophage tropism are determined

distinct cell type-specific fusion cofactors. We applied a recombinant vaccinia virus-based reporter gene assay for Env-CD4-mediated cell fusion; the LAV and Ba-L Envs served as prototypes for T-cell line-tropic and macrophage-tropic isolates, resp. We examined CD4+ promyelocytic and monocytic cell lines that are infectible by T-cell line-tropic isolates and become susceptible to macrophage-tropic strains only after treatment with differentiating agents. We observed parallel changes in fusion specificity: untreated cells supported fusion by the LAV but not the Ba-L Env, whereas cells treated with differentiating agents acquired fusion competence for Ba-L. These results suggest that in untreated cells, the block to infection by macrophage-tropic isolates is at the level of membrane fusion; furthermore, the differential regulation of fusion permissiveness for the two classes of Envs is consistent with the existence of distinct fusion cofactors. To test this notion directly, we conducted expts. with transient cell hybrids formed between CD4-expressing nonhuman cells (murine NIH 3T3) and different human cell types. Hybrids formed with HeLa cells supported fusion by the LAV Env but not by the Ba-L Env, whereas hybrids formed with primary macrophages showed the opposite specificity; hybrids formed between HeLa cells and macrophages supported fusion by both Envs. These results suggest the existence of cell type-specific fusion cofactors selective for each type of Env, rather than fusion inhibitors for discordant Env-cell combinations. Finally, analyses based on recombinant protein expression and **antibody** blocking did not support the proposals by others that the CD44 or CD26 antigens are involved directly in the entry of macrophage-tropic isolates.



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#17	Search CC-CKR5 and CCR5 Field: All Fields, Limits: Publication Date to 1997/12/30	10:27:10	165
#16	Search CC-CKR5 and CCR5 Field: All Fields, Limits: Publication Date to 1998/12/30	10:26:54	382
#15	Search CC-CKR5 and CCR5	10:26:30	2095
#13	Search antibody and 5C7 and chemokine Limits: Publication Date to 1997/05/05	08:55:34	1
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#10	Search antibody and 5D7 and chemokine Field: All Fields, Limits: Publication Date to 1996/06/17	08:54:45	0
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#6	Search antibody and 5C7 and chemokine Limits: Publication Date to 1996/05/20	08:53:59	0
#5	Search antibody and 5C7 Limits: Publication Date to 1996/05/20	08:53:44	7
#2	Search antibody and 5D7 Limits: Publication Date to 1996/05/20	08:53:30	7
#4	Search antibody and 5D7 and chemokine Limits: Publication Date to 1996/05/20	08:53:24	0
#3	Search antibody and 5D7 and R5 Limits: Publication	08:53:16	0



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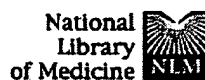
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